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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/331,808	01/27/2000	BJORN H. LINDQVIST	MJW-117-357	2109

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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	**PAPER NUMBER**
1639	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/331,808	LINDQVIST ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *05 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21,22,24-29,34-36,39 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,22,24-29,34-36,39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 21-22, 24-29, 34-36 and 39-40 are pending and under examination.

Withdrawn Rejections

In view of the amendments to the claims and applicants' arguments the 35 USC 112, first paragraph rejection is withdrawn.

Claim Rejections - 35 USC § 112

Claim 40 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 40 is unclear as to the recitation of "NX174" (this appears to be a typographical error).

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 21-22, 24-29, 34-36 and 39-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schatz (5498530) in view of either Derbyshire (Molecular Microbiology) or Liu ((Virology) and Kauffman (6100035).

Schatz discloses in the Examples and figures a method of generating the peptide library which comprises the steps of (a) constructing a recombinant DNA vector that encodes a DNA binding protein and contains binding sites for the DNA binding protein; (b) inserting into the coding sequence of the DNA binding protein in a multiplicity of vectors of step (a) coding sequences for random peptides such that the resulting vectors encode different fusion proteins, each of which is composed of the DNA binding protein and a random peptide; (c) transforming host cells with the vectors of step (b); and (d) culturing the host cells transformed in step (c) under conditions suitable for expression of the fusion proteins. The peptide library produced by this method is especially useful in screening for ligands that bind to a receptor of interest. This screening method comprises the steps of (a) lysing the cells transformed with the peptide library under conditions such that the fusion protein remains bound to the vector that encodes the fusion protein; (b) contacting the fusion proteins of the peptide library with a receptor under conditions conducive to specific peptide-receptor binding; and (c) isolating the vector that encodes a peptide that binds to said receptor. By repetition of the affinity selection process one or more times, the vectors that encode the peptides of interest may be enriched. The recombinant vectors of the random

peptide library are constructed so that the random peptide is expressed as a fusion product; the peptide is fused to a DNA binding protein. A DNA binding protein must exhibit high avidity binding to DNA and have a region that can accept insertions of amino acids without interfering with the DNA binding activity. Suitable DNA binding proteins include proteins selected from a large group of known DNA binding proteins including transcriptional regulators and proteins that serve structural functions on DNA. Examples include: proteins that recognize DNA by virtue of a helix-turn-helix motif, such as the phage 434 repressor, the lambda phage cI and cro repressors, and the E. coli CAP protein from bacteria and proteins from eukaryotic cells that contain a homeobox helix-turn-helix motif; proteins containing the helix-loop-helix structure, such as myc and related; the phage P22 Arc and Mnt repressors (see Knight et al., 1989, J. Biol. Chem. 264(7):3639-3642 and Bowie and Sauer, 1989, J. Biol. Chem. 264.(13):7596-7602, each of which is incorporated herein by reference); and others. Schatz does not disclose that the DNA-binding protein is cis-proteins. However, Derbyshire et al discloses at page 1261 that cis proteins can work up to 1000-fold more efficiently if its gene is located close to is binding site. Liu disclose at page 163 that P2A is the best-studied system where A protein nicks the origin site and forms a covalent

link to the cleaved strand. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to employ cis- protein as the DNA-binding protein in the method of Schatz as taught by Liu or Derbyshire. The advantages in the use of said cis-protein as taught by Liu or Derbyshire would provide the motivation to one having ordinary skill in the art to make the modification at the time the invention was made.

Response to Arguments

Applicants submit that there is nothing in Schatz that would have suggested that such cis-acting proteins should be used. Further, nothing is seen in the cited art that would have motivated an artisan to combine the teachings of Schatz with those of Derbyshire or Liu. The combination would appear to be based on improper hindsight-based reasoning, as evidenced by the Examiner's arguments. Both Derbyshire and Liu are in an unrelated field to protein display and the production of peptide display libraries. Thus, Applicants cannot see why, absent knowledge of the present invention, these documents would have been combined by one of skill in the art as has been done by the Examiner. No suggestion for making that combination is found in the references themselves. Nothing in Derbyshire or Liu would have suggested

that the proteins described in those documents might have any utility in such peptide display libraries.

In reply, applicants' attention is again directed to the disclosure of Schatz above wherein he discloses:

> A DNA binding protein must exhibit high avidity binding to DNA and have a region that can accept insertions of amino acids without interfering with the DNA binding activity. Suitable DNA binding proteins include proteins selected from a large group of **known DNA binding proteins including transcriptional regulators** and proteins that serve structural functions on DNA. Examples include: proteins that recognize DNA by virtue of a helix-turn-helix motif, such as the phage 434 repressor, the ***lambda phage cI and cro repressors***….
> (Emphasis added.)

Claim 40 which recites lambda phage 174 which includes the above lambda phage CI and cro repressors cited by Schatz above. The claimed property of the cis-DNA binding protein is a protein inherent to the DNA binding proteins disclosed by Schatz, which appears to be the same protein, as claimed. As applicants recognized at page 7 of the REMARKS of 12/5/2006, the property of a DNA binding to act as cis-acting is inherent to DNA binding protein. Not just because Schatz does not recite this property of DNA binding protein does not render the claimed method prima facie obvious.

> Where the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of

> his claimed product. See In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same as is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. See In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972); In re Best 195 USPQ 430 (CCPA 1977).

The Office does not have the facilities and resources to provide the factual evidence needed in order to establish as to the inherent property of the cis-DNA binding proteins. In the absence of evidence to the contrary, the burden is upon the applicants to prove that the claimed cis-acting DNA binding protein produced by the claimed process are different from those taught by the prior art and to establish patentable differences. See In re Marosi, 218 USPQ 282, 292-293 (CAFC 1983); In re Thorpe, 227 USPQ 964 (CAFC 1985).

Applicants in effect, are arguing that a structure suggested by the prior art, and hence potentially in possession of the public, is patentable to them because it also possesses an inherent, but hitherto unknown property, which they claim to have discovered. This is not the law. A patent on such structure would remove the public that which is in the public domain by virtue of its inclusion, or obviousness from the prior art. In re Wiseman 201 USPQ 658.

In response to applicants' argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

It is not clear why the disclosure of Derbyshire (page 1261) that cis proteins can work up to ***1000-fold more efficiently if its gene is located close to is binding site***, would not provide a motivation to one having ordinary skill in the art. If such proteins are 1000-fold more efficient, especially when near its binding site, like cis-proteins hence, one having ordinary skill in the art would be motivated to use a compound that has been found in the art to be ***1000(!!) more efficient*** than other, further away DNA binding proteins.

Derbyshire is employed not for the purpose as argued i.e., to disclose protein display. Rather, it is employed for the purpose why one having ordinary skill in the art would choose cis proteins over the other known cis-acting DNA protein.

Applicants state that the above statement of Derbyshire merely relates to cis-acting proteins per se and how such proteins might act in the most efficient manner. It does not suggest that cis-acting proteins might in some way be more efficient or have some advantage over the proteins described in Schatz. Derbyshire does not teach an advantage in the use of cis-acting proteins but merely presents a statement of fact relating to cis-acting proteins, namely that they work a 1000-fold more efficiently if its gene is located close to its binding site.

In response, the statement of fact provided by Derbyshire would suffice to motivate one having ordinary skill in the art to use a more efficient DNA binding protein in the method of Schatz. This is especially true since Schatz teaches that any DNA binding protein (as the claimed phage) is applicable to the method of Schatz and as claimed i.e., a general method of producing a library of any protein.

In addition, the disclosure of Liu that said cis-acting DNA protein is the best-studied system would provide more than a lead or motivation to employ said protein.

It is well settled that there is no requirement that a motivation to make the modification be expressly articulated. The test for combining references is what the combination of

disclosures taken as a whole would suggest to one of ordinary skill in the art. In re Simon 174 USPQ 114 (CCPA 1972).

As a whole the dual benefits obtained in using a cis-acting DNA protein as taught by Derbyshire and Liu would lead one having ordinary skill in the art to the claimed method using the known cis-acting DNA binding protein.

Thus, the disclosure of Schatz, even alone, would suggest the claimed method. Schatz discloses the same method and recites lambda component comprised in the claimed lambda 174. DNA binding protein, as applicants acknowledge has its inherent property to act as cis-acting DNA binding protein. Kaufmann further evidences this

> Kaufmann discloses at col. 4, line 10 up to col. 5, line 25:
>
> The term "cis acting nucleic acid element" refers to a single-stranded or double-stranded RNA or DNA sequence that can be selectively bound by nucleic acid binding factors to regulate one or more genetic activities of a nucleic acid sequence present on the same molecule. ***Cis acting nucleic acid elements are present in all organisms, including prokaryotes, eukaryotes and viruses.*** For example, cis acting nucleic acid elements are present in yeast, animals, plants, bacteria and viruses. (Emphasis ours.)

Claims 21-22, 24-29, 34-36 and 39-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gold (WO 92/02536) in view of Kauffman (6100035).

Gold discloses a method of identifying a protein or peptide comprising of preparing an amplifiable gene library of DNA molecules which contain a nucleotide sequence that encodes proteins such as that it binds to the DNA encoding sequence through covalent protein-DNA binding and to which the encoded peptide sequence is display and expressing the genetic library formed. See Gold at e.g., page 9, lines 14 up to col. 19 and the Examples. Gold does not teach that the DNA binding protein is cis-acting DNA protein.

Kaufmann discloses at col. 4, line 10 up to col. 5, line 25:

> The term "cis acting nucleic acid element" refers to a single-stranded or double-stranded RNA or DNA sequence that can be selectively bound by nucleic acid binding factors to regulate one or more genetic activities of a nucleic acid sequence present on the same molecule. Cis acting nucleic acid elements are present in all organisms, including prokaryotes, eukaryotes and viruses. For example, cis acting nucleic acid elements are present in yeast, animals, plants, bacteria and viruses. See also col. 28, lines 33-60.

Accordingly, the DNA encoding protein of Gold is an inherently cis-acting protein since as taught by Kaufmann this cis-acting DNA protein are present in all organism including bacteria and viruses as the claimed P2A which is found in bacteriophage.

No claim is allowed.

Conclusion

Nguyen (7138511) discloses cis elements.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571)272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571)272-0763. The fax phone number for the organization where this application or proceeding is assigned is(571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

Tdw

April 9, 2007